Comments and Suggestions for Revision of the 2009 Draft Guideline for the Prevention of Intravascular Catheter-Related Infections

Thank you for the opportunity to provide comments on this draft guideline.

Major Comments:

First, there is no discussion or explanation of how the various individuals were selected to be authors of this guideline. Some have published extensively in this area and others have published nothing in this area. Are they members representing different organizations, etc.? For example, I find >25 references cited where Dr. Dennis Maki is an author and yet he is not a member of this group. Was an effort made to identify the leaders in the field of research of preventing catheter-related infections (CR-Is) and recruit them to be on this committee? Some explanation of the process of selecting the members of this committee would be appropriate to include in the introduction.

Second, it is unfortunate that this revision was not coordinated with the release of the Society for Healthcare Epidemiology of America's (SHEA) compendium in October 2008. The release of multiple guidelines by multiple organizations with varying recommendations leads to confusion and chaos in the infection control community and impedes implementation of evidence-based practices, particularly when they are rated differently (Category 1A, 1B, II and unresolved issue) by the different groups.

Third, many of the references cited do not provide data to substantiate the level of recommendation being provided. Please provide the specific references that led you to provide the level of recommendation, so the reader can see the data and make their own judgment on the level of evidence. In many instances, the references cited do not seem to be appropriate and seem to be just copies of the 2002 guideline, where they were also not appropriate. Have the authors actually read these references and determined that they have the data to lead to the recommendations being made. Since the guideline emphasizes the importance of their level of recommendation, the authors should insure that the data in each paper cited actually addresses the issue in question and provides sufficient data to lead to the level of recommendation being made. Merely cloning from the 2002 guideline may not be appropriate, as many of the references used in that guideline either did not address the question or did not provide data to support the level of recommendation. I would recommend that one or more committee members read each reference being cited for a specific recommendation to insure that both the issue is addressed in the recommendation and the level of support is provided to justify the level of the recommendation.

Fourth, you reference to 80,000 CR-BSIs in ICU patients and 250,000 CR-BSIs in hospital patients. These are the exact same data as used in the 2002 guideline. It is hard to believe that these numbers have not changed in nearly a decade. Also, you refer to these as if these are definitive numbers. Both are gross estimates from CDC's NNIS/NHSN (made nearly 10 years ago). With the ICU data, <350 hospitals (of >5,000) in the United States were included at the time of this estimate. For the hospital-wide

estimate of CR-BSIs, this is an even more indirect estimate. At the time of this estimate, the NNIS/NHSN system did not include hospital-wide data. This estimate was made by multiplying NNIS/NHSN data by National Hospital Discharge Summary (NHDS) data—notoriously inaccurate for HAIs. Thus, rather than referring to these as solid data, you should indicate that these are **gross estimates** and that solid data on the true magnitude of CR-BSIs in ICUs or hospital-wide are unknown or provide new updated numbers or estimates.

Fourth, I find it amazing that there is not a single word about the inappropriateness and inaccuracy of the use of the CDC's NNIS/NHSN method of determining the denominator for calculating the CR-BSI rates. In NNIS/NHSN, each patient in the ICU with one or more central lines is counted as one central line day each day. It does not matter if the patient has >1 central lines or one or more lines with multiple lumens. There are papers (not cited in this Guideline revision), that show that the CR-BSI rate varies with the number of central lines and with the total number of lumens. The current methods originate from studies published in 1990 using NNIS data from the 1980s—at a time when many or most patients had one central line, often with one lumen. Don't you think it is time to use a more accurate determination of central line days and for calculating the CR-BSI rate using either the total number of catheter-days (all the patient has) or lumen-days (all the patient has)? The current method penalizes tertiary care centers, where they over-estimate their CR-BSI rate using this method.

Fifth, although the criteria for different levels of recommendation (i.e., **Category IA.** Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.
Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies, and a strong theoretical rationale.
Category IC. Required by state or federal regulations, rules, or standards.
Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.
Unresolved issue. Represents an unresolved issue for which evidence is insufficient or no consensus regarding efficacy exists) are clearly outlined, there seems to be considerable arbitrariness in the application of Category 1A, 1B, or Category II. A more reproducible and rigorous criteria system of recommendation classification is needed. For example, a Category 1A is given for healthcare worker education, yet there are only two studies of physician education on CR-BSI rates (e.g., Sherertz et al and Eggimann et al), neither of which were randomized controlled trials, addressing this. Some of the other studies referenced are underpowered studies (most before/after or just anecdotal reports) of nurses training. There are at least three randomized controlled trials of use of IV or PICC teams—which some could say is correlated with education and competetancy (Nehe JAMA 1980, Tomford 1984, Edlin 1998) that are not even cited and no recommendation for IV/PICC teams is made. Other interventions have multiple studies (use of prophylactic antimicrobials in neonates at catheter insertion) or many randomized controlled trials (CHG-impregnated sponge or antibiotic locks/flushes) yet they do not receive a Category 1A recommendation or are recommended against. Clarification of what constitutes "supported" vs. "strongly supported" is needed, as the decision to give a

Category 1A vs. Category 1B vs. II recommendation seems arbitrary and capricious. The lack of standardization of application of these criteria (esp. Categories 1A, 1B and II) is a major issue that needs to be addressed.

Sixth, your recommendation on the CHG-impregnated sponge seems to have ignored the 14 randomized controlled trials and meta-analyses assessing the efficacy of this technology in preventing CR-BSIs, local site infections and reducing local site bioburden. You should be referencing these studies, especially as you do not cite any of these studies. Fourteen randomized controlled studies (and many other case-control or cohort studies) have been published. The studies include: Garland 2001, Karwawska 1998, , Levy 2005, ;Crawford, Chambers 2005, Egol 2005, Mann 2001, Shapiro 1990, Roberts 1999, Hanasaki 1999, Wu 2008, Timset 2008, Reschulte 2008. In particular, the Reschulte and Timset articles (both randomized controlled trials) were published after the SHEA Compendium was published. The Reschulte paper (Ann Hem 2008) shows that the CHG-impregnated sponge or BioPatch reduces CR-BSI rates in oncology patients even if the insertion bundle and antiseptic-impregnated catheters are used. The Timset (JAMA 2008) paper shows that even with a low CR-BSI rate in ICUs (1.3 per 1,000 CVC-days) and use of the insertion bundle, that they still resulted in a statistically significant reduction in CR-BSI rates in these patients with introduction of the CHG-impregnated sponge or BioPatch. Last, I understand that Drs. Sadfar and Maki have completed a meta-analysis of the randomized controlled trials evaluating the CGH-impregnated dressing or BioPatch and have found that this intervention results in a statistically significant reduction in CR-BSIs. You may want to contact them to see if you can see this latest meta-analysis.

In addition, since some are using silver impregnated dressings or other CGH-impregnated dressings (both with no published clinical efficacy data), you might want to address these in your recommendations.

Seventh: Your section on needleless connectors needs considerable rewording, revison and correction. The recommendation on connector disinfection fails to include all available data (and makes a recommendation for an FDA-approved antiseptic for use as a disinfection and ignores the data on use of 70% alcohol or CHG and the need to scrub the hub for at least 15 seconds. A more comprehensive discussion of the various types of needleless connectors is needed and expansion of this section is important. Use of antimicrobial or antiseptic locks for these devices should be recommended based upon the data. Specific data on the risk of CR-BSI with negative or positive pressure/displacement leur access mechanical valve needleless connectors should be provided and more precise recommendations made.

Eighth, you should expand your recommendations on prevention of CR-BSI in hemodialysis patients. You have literally one recommendation for the population that has the highest risk of CR-BSI of any population. You should recommend against the use of catheters (vs. fistulas or shunts), use of antiseptic/antimicrobial lock, etc.

Specific Comments:
Page 4, line 88: The number of 80,000 s in ICUs is an **estimate** (derived from the CDC's NNIS systems. At the time of these estimates, <350 hospitals were participating in NNIS/NHSN. Thus, rather than writing this as if it is a definitive and accurately derived number of CR-BSIs in all U.S. ICUs, indicating that this is an estimate (and that we do not have very accurate data) derived many years ago (before most of the CR-BSI prevention bundles were introduced), would be more appropriate. Furthermore, a more recent estimated based on more current, direct and accurate data would be preferred. In addition, the **estimate** of 250,000 healthcare-associated CR-BSIs nationally is even more of an estimate, as neither NNIS nor NHSN include hospital-wide surveillance for HAIs at the time of this estimate and thus this estimate is made from extrapolations and data from the NNIS/NHSN and the National Hospital Discharge Survey (estimates made from two systems that are indirect estimates of the actual data). Again, it would be better to indicate that these are gross estimates and that there are no solid data on the true number of HA-CR-BSIs in ICUs or hospital-wide.

Page 4: Shouldn't you point out that all or most of the successful interventions targeting CR-BSI rates of zero have been conducted in ICUs and that the need is for programs that target hospital-wide efforts and whether the current bundles (for example without IV teams) will be successful hospital-wide is unknown. I do not think that we can just extrapolate from ICUs to hospital-wide efforts and the likelihood of success. Personnel, I believe that IV/PICC teams will be necessary for hospital-wide success.

Pages 5-7, lines 119-158: Shouldn't you specify what personnel should do to work-up a patient with a potential bloodstream infection or sepsis? At the least reference, the IDSA and CSI guidelines recently published for diagnosis and management of CR-BSIs. Since it is very difficult to get many clinicians to draw a central and a peripheral culture when evaluating a patient with potential BSI, it would be helpful to, at a minimum, include this in your recommendations and discussion.

Page 7, line 158-159: I find it incredible that CDC and HICPAC can recommend 5-7 methods of calculating MRSA rates, but continues to use the old methodology for calculating CR-BSI rates. There are data to show that when one has >1 CVC, that the risk of CR-BSI increases. In addition, there are data to show that with >1 lumen catheter, the risk of CR-BSI increases. Virtually all clinicians I speak to agree that CR-BSI risk increases with the number of CVCs and with the number of lumens. Yet, you recommend that each patient with one or more CVCs with one or more lumens be counted as one CVC-day (see line 139, page 6). This approach penalizes large tertiary care centers and over-estimates their CA-BSI rate. At a minimum, there should be discussion of the need to capture the true number of CVCs and/or lumens and use that for determining CR-BSI rates. To continue to ignore this huge confounding variable is scientifically unsound. Furthermore, the references given for calculating the CR-BSI rate from the JC (not JCAHO, as you indicate, anymore) and from the CDC's NHSN have no data on the validity of the approach and ignores data documenting that this approach is not valid. The recommendation for the current approach was made in 1990 based on data from 1980-1990. At that time, many if not most ICU patients had one central line and

one lumen. The current situation in ICUs is very different, as most patients have >1 central line and >1 lumen. If such a recommendation for changing the approach to calculating the denominator for CR-BSI is not made, then you should at least explain why you are not making such a recommendation. Science rather than tradition should be the determinants of this guideline. How can you include a paragraph discussion of the differences between catheter-related BSI and catheter-associated-BSI and ignore the fact that the denominator used for calculating the rate is not appropriate?

In addition, it is well-known that the risk of CR-BSI differs by the type of catheter used (CVC—tunneled vs. non-tunneled, PICC, etc.), yet the CDC NHSN does not differentiate CR-BSI rate by catheter type. I suspect much of the decrease in CR-BSI rate during the late 1990s and 2000s in NHSN hospitals was merely the increased use of PICCs (with lower risk of CR-BSI) and a decrease in the use of CVC (with their higher risk of CR-BSI). If catheter type data are not collected and CR-BSI rates calculated by at least CVC vs. PICC, a major confounder of CR-BSI rates will continue and it will make it even more inappropriate to use benchmarking and comparisons across institutions.

Page 7, line 166-168: Can't you include more up-to-date data? This guideline will be published in 2010 (at the earliest) and by that time, these data will be at least three years old. Given the major efforts being made to reduce CR-BSIs in ICUs, I suspect the rates have declined and these data do not accurately reflect the current state of CR-BSI prevention.

Page 7-8, line 169-173: Personnel should be discouraged from using NHSN data as a benchmark. There should be a goal of 0 BSIs per 1,000 CVC-days, not just being at or slightly below the median NHSN rate. Furthermore, as indicated above, since you are not capturing the actual number of catheters or lumens nor type of catheter PICC vs. CVC), a large number of confounders are not controlled in the NHSN data and hospitals should be strongly encouraged to compare their own rates over time and strongly discouraged from comparing (inter-facility) their CR-BSI rates to NHSN. Such comparisons not only ignore the above, but fail to take into account the type of needleless connector (e.g., split septum vs. luer access mechnical valve—negative, neutral or positive pressure), whether there is an IV or PICC-team (documented to reduce CR-BSI rates), distribution of catheters by site of insertion and catheter type, and use of other CR-BSI prevention interventions (e.g., impregnated catheters, CHG-impregnated sponge, CHG bathes, antibiotic or antiseptic locks or flushes, etc.). Without knowledge of all of these things, it is epidemiologically and scientifically unsound to make comparisons to benchmarks.

Page 8, lines 175-188: These data will be >4 years old by the time this guideline is published. Please provide more up-to-date data. Antimicrobial resistance references (17 and 18) will be 4-5 years old by the time this guideline is published. Please update.

Page 8, line 193: The reference 18 (Burton) presents data from NHSN on decreasing CR-BSI rates, but does not present (nor do they know) what prevention interventions (if any) were implemented in these hospital ICUs. At a minimum, you should include several of

the huge number of publications illustrating how to decrease MRSA-BSI-rates (Huang et al CID, Muder et al ICHE, Robechek et al Annals of Internal Medicine).

Page 9, line 197-205: These CDC data are 6 years old. You might want to include the reference of Jefferies et al (ICHE-2009), a multi-center Children's Hospital Corporation of America (CHCA) collaborative to reduce CR-BSIs in Pediatric ICUs, or other more current data from the CDC or published data. The CHCA and NACHRI intervention showed the importance of use of an insertion bundle and the NACHRI intervention recently has shown the importance of an insertion and a maintenance bundle.

Page 9, 204: Catheter utilization rates are grossly confounded by the fact that you are not collecting the actual number of catheters and/or lumens in both adult and pediatric ICU patients. Furthermore, these are data published in 1999 (a decade ago). Please update with more current and useful data.

Page 9: The use of CVC-days (as currently used), ignoring both the type of catheter, the number of catheters and the number of lumens actually used, was recommended by CDC in 1990 (Jarvis et al AJM 1990), based upon data from 1980-1990. Isn't it time to control for additional confounding variables (at that time it was catheter use and duration of catheterization) and now include the actual number of catheters used and at a minimum the type of catheter (PICC vs. CVC)? It is time to advance the field rather than totally ignoring these important issues. We should be evidence-based rather than tradition-based in our recommendations.

Page 9, line 206-211: Why are you referencing 1999 data in 2009/2010? Update to more current and relevant data. Furthermore, references 22 and 23 were not designed to assess the pathogens causing CR-BSI but rather were to assess the BioPatch (22) or vancomycin-heparin flushes in neonates (23). Please update with current NHSN data.

Page 10, line 220 to page11, line 254: You may want to point out that although all invasive devices have a biofilm by the time they are present for 12-24 hours, that only a minority of these patients will develop a CR-BSI and that we do not understand the additional specific factors that lead to the CR-BSI in addition to the presence of biofilm.

Page 11, lines 259-262 and page 12, lines 263-264 (recommendations 1 and 2): Although I agree that this is important, I do not believe there are sufficient clinical or epidemiologic studies (certainly no randomized controlled trials) to make this a Category 1A. A Category 1B recommendation would seem more reasonable. Just because we believe it (dogma), does not make it so (data). In addition several of these references do not specifically address the issue of education and its impact on CR-BSI. Reference 53 is on surveillance. References 56 and 57 are from the same institution over the same period of time and may include the same patients. References 60 and 61 address physician education. You have virtually no references addressing nursing clinician education and its impact on CR-BSI.

Page 11, line 265-266 and page 12, line 276-278: Given your statement that "Specialized "IV Teams" have shown unequivocal effectiveness in reducing the incidence of catheter-related infections", why have you not made a Category 1A recommendation for IV/PICC teams. At least two of the studies assessing IV teams are randomized controlled trials (please add the study by Dr. Brian Edlin). Shouldn't such data and your statement lead to a Category 1A recommendation for IV/PICC teams? Given the mandate to reduce CR-BSIs hospital-wide, this would seem to be an appropriate recommendation.

Page 12, lines 263-266: The data for recommendations #2 and3 are relatively weak. It seems inappropriate to make them a Category 1A recommendation and make the staffing ratios a recommendation Category 1B. I believe #2 and 3 should be Category 1Bs, as most are before/after studies and not randomized controlled trials and many were multifaceted interventions not solely education or periodic evaluation of knowledge.

Page 12, line 269: Add the publication by L. Archibald et al illustrating the importance of nurse to patient ratio on CR-BSI risk in pediatric patients.

Page 13, line 285-286, the references cited for this recommendation (82 and 83) do not seem appropriate. Neither are studies in pediatric patients. One is a summary article (no original data). The other is a selected study in oncology patients (mostly adults). Studies specifically performed in pediatric patients should be used to make this recommendation. The currently cited references do not seem sufficient even for a Category II recommendation.

Page 13, line 287-289, the references for this recommendation (83-85) do not seem appropriate. Two are summary or opinion pieces. The other is a selected study in oncology patients. These do not seem sufficient for a Category 1B recommendation.

Page 13, line 290-291, the references for this recommendation do not seem appropriate. One is a review type article (85), one is a retrospective study in oncology patients, and the third is a before/after study. These do not seem sufficient for a Category 1A recommendation.

Page 13, line 292-294, the references for this recommendation do not seem appropriate. Two are summary or opinion pieces. The other is a selected study in oncology patients. These do not seem sufficient for a Category 1B recommendation.

Page 13, line 301-302, reference 25 does not seem appropriate here. It refers specifically to Swan-Ganz pulmonary arterial catheters not central venous catheters. Reference 100 is on mechanical complications not CR-BSIs. None of the references seem sufficient to give this recommendation a Category 1A.

Page 13, line 305-307: Shouldn't you make a specific recommendation <u>against</u> using catheters rather than shunts or fistulas for hemodialysis, given the much higher rate of CR-BSIs associated with central catheters?

Page 14, line 307-309: Rather than just providing meta-analysis (reference 107), you should be providing the original studies that actually lead to this recommendation being a Category 1B and are included in the meta-analyses. Did you actually read the papers in the meta-analysis or just assume the analysis was done correctly (usually some arbitrary inclusion and exclusion criteria for such analyses). Furthermore, are there any data to support this recommendation for pediatric patients? I have been told that at least in neonates, the insertion of a PICC usually does not require the use of ultrasound, as the vessels are easily visualized, particularly in low birth-weight neonates (experience is more important than ultrasound). If there are any data to support this recommendation in pediatric or neonatal patients, it should be provided.

Page 14, line 310-311: The two references do not support a Category 1A recommendation. These were multifaceted interventions that did not singly evaluate the impact of removing catheters when they were no longer essential. Although I agree with the concept of doing this, there are no data to support that this recommendation be given a Category 1A (not really any data to even give it a Category 1B). I am not aware of any study that has evaluated this intervention alone. It has always been a part of an insertion bundle that included many interventions simultaneously.

Page 14, line 326-329: It might be useful to quote some data on bioburden at these various sites. Culture studies show 10^2-10^3 cfu/cm^2 for the antecubital fossa, 10^4-10^5 cfu/cm^2 at the subclavian site and 10^6-10^8 cfu/cm^2 at the femoral site. Perhaps, if clinicians understand the different bioburdens exist at these various sites, it will help them preferentially inset catheters at lower risk sites.

Page 15, line 347-352: Rather than just providing meta-analyses, you should be providing the studies supporting your statements regarding use of ultrasound for catheter placement. Furthermore, are there any data to support this recommendation for pediatric patients? I have been told that at least in neonates, the insertion of a PICC does not need use of ultrasound. If there are any data to support this recommendation in pediatric or neonatal patients, it should be provided.

Page 16, Line 362-364: I do not believe these references (124-6) support these statements. The first (124) is a study of colonization of catheters. The second (125) is on phlebitis with catheters. The third is on dressings and PICCs. None of these address the risk of infectious complications associated with different types of catheters. Nor are any of these studies comparisons of infectious complications (CR-Is or CR-BSIs) associated with catheters made of different materials.

Page 16-17, lines 371-377: None of these studies show that performing hand hygiene as recommended reduce CR-BSIs. The first (reference 58) is a study of HCW education. The second (reference 127) is the hand hygiene guideline. Reference 129 is a comparison of impact on skin of different hand hygiene agents. Most egregious is the use of reference 131 as this study by Bryan Simmons while he was at the CDC, which in fact, shows no decrease in HAIs when hand hygiene was enhanced. In addition, there is a study by Rupp et al published in 2009 that shows no decrease in HAIs with enhanced

hand hygiene. Although I agree that hand hygiene is important, it is critical that an evidence-based guideline use data to support the recommendations being made. These references do not do that; they do not justify giving this recommendation a Category 1A level of recommendation. Not a single randomized controlled trial or even a quasi-experimental study shows the impact of hand hygiene in a non-multifaceted intervention study on CR-BSI rates. Also, all evidence-based data should be referenced (e.g., Rupp study), not just those supporting the point. Is this recommendation based upon data or dogma?

Page 17, lines 378-379: I do not believe any of these references provide data to document aseptic technique decreases CR-BSI rates. The first (reference 25) is on Swan-Gantz pulmonary artery catheters. Reference 132 is on use of maximum barrier precautions. Reference 133 is in hemodialysis patients (who shouldn't have a central line unless a shunt or fistula is impossible). Reference number 134 is use of IV teams and dressing changes. None of them specifically compares use of aseptic technique alone on CR-BSIs. These studies do not support a Category 1A recommendation, even though we all agree that use of aseptic technique is preferred. None of these studies was published after 1999. Aren't there any recent data to support this recommendation?

Page 18, lines 399-403: Aren't there any more recent data on the benefit of maximum barrier precautions (MBP)? The data cited do not seem sufficient for a Category 1B recommendation. Reference 60 is the Sherertz study of the impact of education (not MBP); I do not believe this study, as you indicate, focused "especially MSB". Reference 132 is Dr. Raad's randomized controlled trial in oncology patients (><500 patients total). Reference 136 addresses catheter colonization not CR-Is. Reference 137 addresses Swan Gantz catheters and is from 1994. Surely, there are more recent data to support the use of MBPs and perhaps to increase the recommendation to a Category 1A.

Page 19, lines 424-426: Why would you recommend one type of skin preparation for peripheral catheter insertion (70% alcohol) and another for CVCs (2% CHG)? Skin antisepsis is skin antisepsis; it does not change with the type of catheter or location of insertion. How does this achieve a Category 1A recommendation based on one study? Also, could you address the issue of different concentrations of CHG? Is 2% required? Reference 142 assesses 0.5% tincture of CHG not 2% CHG. Please address different CHG concentrations with or without alcohol and povidone iodine with or without alcohol. Your recommendation for skin antisepsis does not seem to take into account current data.

Page 19, line 430: The use of CHG for skin preparation in NICUs is critically important. A number of NICUs are and have been using CHG, even in low birth-weight infants. For example, I believe that the NICU at Columbia University in New York City is using CHG for skin prep in all their infants with no adverse impact.

Page 19, lines 432-436: Isn't it really the fact that most CHG preparations for skin antisepsis are combinations of alcohol and CHG. It is the alcohol that has the immediate impact and CHG which has the slower and residual impact. Re-word this recommendation so that clinicians do wait for the CHG to dry; by saying that CHG works

on contact, many may feel they do not need to wait for any drying. I do not believe that either of your references (140 or 141) assessed the impact of allowing the CHG to dry vs. not allowing it to dry. Also wouldn't it be more accurate and evenhanded to point out that the trials of CHG vs. alcohol have been CHG with alcohol vs. Povidone iodine without alcohol. Povidone iodine with alcohol may be just as effective as CHG with alcohol. Please include all the studies referenced in the meta-analysis, not just the meta-analysis itself.

Page 20, lines 459-460: These references are very old. Please update with more recent data.

Page 20, line 463-464: Do these references actually examine replacing vs. not replacing and show an increase CR-I rate? I do not believe these data warrant a Category 1B recommendation. Again, dogma vs. data.

Page 20, line 465-367: I do not believe these references address this issue specifically. Also, does it make sense to you that use of ointments would be efficacious in one population with catheters (hemodialysis), but not in others with long-term catheterization?? This seems illogical to me. Again, I do not see where these references lead to a Category 1B recommendation.

Page 21, lines 468-471: Add the reference by C. Toscano et al in ICHE 2009. This is a more recent reference than any you include. Now, there are at least three quasi-experimental studies showing that exposure to water sources can lead to CR-BSIs. Does this lead to a Category 1B recommendation?

Page 21, lines 472-475, add the paper by Timsit et al (JAMA-2009), which assessed the impact of dressing changes at 3 and 7 days.

Page 21, line 480-481: One study leads to a Category 1B recommendation?

Page 21, lines 483-486: It is unclear to me how you determine your level of recommendation. As indicated many times above, you have a Category 1B recommendation based on one study or a Category 1A recommendation based on 2-3 opinion pieces, quasi-experimental studies, etc. To date, there have been at least 14 randomized controlled trials (more than anything else you are giving a Category 1A recommendation to). You should be referencing all of these studies. The 14 randomized controlled studies (and many other case-control or cohort studies) have been published. In addition to the Garland (22), Timsit (156), Ho (157) and Levy (157) studies, you should cite the following additional references: Karwawska 1998, Crawford, Chambers 2005, Egol 2005, Mann 2001, Shapiro 1990, Roberts 1999, Hanasaki 1999, Wu 2008, and Reschulte 2008. In particular, the Reschulte and Timset articles (both randomized controlled trials) were published after the SHEA Compendium was published. The Reschulte paper (Ann Hem 2008) shows that the CHG-impregnated sponge or BioPatch reduces CR-BSI rates in oncology patients even if the insertion bundle and impregnated catheters are used. The Timset (JAMA 2008) paper shows that even with a relatively low

CR-BSI rate in ICUs (1.3 per 1,000 CVC-days) and use of the insertion bundle, that they still found a statistically significant reduction in CR-BSI rates in these patients with introduction of the CHG-impregnated sponge or BioPatch. Last, I understand that Drs. Sadfar and Maki have completed a meta-analysis of the randomized controlled trials evaluating the CGH-impregnated dressing or BioPatch and have found that this intervention results in a statistically significant reduction in CR-BSIs. You may want to contact them to see if you can see this latest meta-analysis. Given the amount of data documenting the efficacy of this intervention (assessed independently of companies, assign with or without the use of the CHG-sponge [thus removing the impact of the other simultaneously included interventions], and published in peer-reviewed publications, I do not understand why this is not given a Category 1A recommendation. Other interventions with far less data are given Category 1A recommendations.

In addition, since some are using silver impregnated dressings (without any clinical efficacy data) or other CGH-impregnated dressings (again, with no published clinical efficacy data), you should specifically address these in your recommendations.

Page 21, line 488: Reference to "visual inspection of the site" should be explained. Many may interpret this as indicating that visualization of the site is recommended for prevention of CR-BSIs. I am aware of no data to support this statement. Furthermore, there are data to indicate that visualization does not predict CR-BSI. So, the fact that one can visualize the site is irrelevant to CR-BSI prevention and such should be stated.

Page 23, lines 520-525: I understand that Drs. Sadfar and Maki more recently have completed another meta-analysis of the randomized controlled trials evaluating the CGH-impregnated dressing or BioPatch (includes additional data to the meta-analysis you are referring to) and have found that this intervention results in a statistically significant reduction in CR-BSIs. You may want to contact them to see if you can see this latest meta-analysis. The latest available data should be used in your guideline.

Page 24, line 539: Add the recent reference by Climo et al (CCM 2009). There are now two studies showing a decrease in VRE-colonization and VRE-BSI with the use of this approach. Perhaps you should consider a specific recommendation for prevention of VRE-BSI using this approach with a Category 1B recommendation in addition to your current recommendation which you could leave for all other pathogens. In addition, you may want to point out that the BSIs that were reduced in reference 162 were VRE-BSIs primarily.

Page 24, lines 552-558: I do not believe there are any good data on use of these devices to reduce CR-BSIs. There are data that they may be useful for mechanical purposes or to protect inadvertent displacement of the catheter. None of these studies are powered sufficiently to assess CR-BSI risk. The reference cited is refers only to PICCS. If you decide to keep this citation, then the limitations of this study—only PICCs, underpowered, etc. should be mentioned. I think it would be more appropriate to comment that there are virtually no data that such devices actually reduce CR-BSI (they may be useful—as mentioned above—for other purposes). Furthermore, there are additional underpowered

studies that have not found that these devices reduce CR-BSIs. They should be referenced.

Page 25, line 564-565: Do not encourage benchmarking. The institutional goal should be zero. People should be comparing their own CR-BSI rate over time. If the rate is not decreasing, they should be doing more. Why do you not include use of the CHG-sponge in the basic comprehensive strategy when it has more randomized controlled studies than MSB or education.

Page 28, lines 637-641: Given that two studies show that systemic antibiotic prophylaxis is protective of CR-BSI, is it appropriate to recommend against it? You have not done this with any other area or recommendation. In this area, you delve into the size of the studies, study population heterogeneity (this did not exist in the CHG vs. alcohol skin prep or antiseptic/antimicrobial vs. non-impregnated catheter meta-analyses???), how many ended the prevention prematurely, etc. On line 655, you indicate that a "recent Cochrane review concluded that there is insufficient evidence from randomized controlled trials to support or refute the use of prophylactic antibiotics". I would argue that this would be the case for nearly all your Category 1A and Category 1B recommendations. Does this imply that only sufficient randomized controlled trials will meet your Category 1A level of recommendation? If it does, then you need to change all the ones you have in the document so far. You have not taken this approach (listing the limitations of the studies) in any other area or study thus far until this section. Seems that this is editorializing in order to justify your recommendation, esp. in the neonatal population where the data support its use.

Page 30: Antimicrobial/antiseptic ointment: Again, seems illogical that this would work for dialysis patients, but not others. Either it does or it does not. A catheter is a catheter; who it is in should make no difference.

Page 31, lines710-712: It is unclear tome how this receives a Category II recommendation, when you acknowledge in your discussion that at least 10 studies (including randomized controlled studies) have been conducted in hemodialysis patients and "three meta-analyses have all demonstrated that catheter lock solutions reduce risk of CR-BSI in hemodialysis patients". How does this get a Category II recommendation and hand hygiene and healthcare worker education (two of several areas that you have given a Category 1A recommendation to) have no randomized controlled trials and much less actual scientific evidence (rather than dogma) to support them? Should you make a specific recommendation for use of this approach in hemodialysis patients, a population with the highest rate of CR-BSI and where few interventions have been successful in reducing this high rate of infection? A similar situation exists for oncology patients. The data should lead to the recommendation. Potential adverse effects are very different than proven adverse effects. The majority of potential adverse effects that you list are theoretical, but not documented in the various studies cited. If you have studies to document the potential side effects (toxicity, allergic reaction or emergence of resistance). Given the problem with negative and positive pressure mechanical valve needleless

connectors, use of antimicrobial or antiseptic lock may reduce the risk of CR-BSI associated with these devices.

Again, this raises questions about how you determine the level of recommendation. An area with randomized controlled trials and meta-analyses demonstrating efficacy receives a Category II (virtually don't do it) recommendation, while dogma area (hand hygiene, education, etc.) with much less robust studies (and no randomized controlled trials or meta-analyses), receives a Category 1A. This does not to be scientific evidence driven categorization.

If you avoid recommending antimicrobial/antiseptic locks or flushes because there is no FDA-approved formulations, then you should not be recommending use of CHG for use as an antiseptic (so you should delete this recommendation) and perhaps develop another level of categorization for interventions that have evidence to support their efficacy, but which cannot be recommended because the FDA does not approve them. Consistency in this guideline is critical.

Page 37, lines 843-847: You may wish to reference the IDSA and CSI guidelines for evaluation of patients with potential sepsis/bacteremia to guideline clinicians on the appropriate work-up of such patients. There is no reference cited for the Category 1B recommendation on line 983-844. Please provide the data upon which this recommendation is based.

Page 40, lines 905-912: Because of their documented higher risk of CR-BSI, shouldn't you make a specific recommendation not to use central lines (vs. shunts or fistulas) for hemodialysis unless absolute essential. You indicate the use of central catheters for hemodialysis is the major risk factor for CR-BSI, but you do not recommend against their use. Without such a recommendation, there will be a continuation of the trend over the past 10-15 years of increasing use of catheters for hemodialysis.

Also, as mentioned above, I believe you should recommend the use of antimicrobial or antiseptic locks and flushes in this population.

This is the highest CR-BSI risk group and there are no recommendations specific to this population to decrease this risk. Please explain why.

Page 42, lines 950-951: I do not believe reference 151 addresses this issue. Reference 151 is a study of subcutaneous cuffs and reference.

Page 46, lines 1050-1052: Please provide the data for this Category 1A recommendation. Our study (reference 321) does not support this recommendation. Our investigation documented extrinsic contamination of propofol by anesthesiologists, not a problem with length of time of infusion. An in vitro study by Arduino et al assessed the growth characteristics of a variety of organisms when extrinsically inoculated into propofol. This may be a better or additional reference to support this recommendation. Regardless, I am not sure that one study supports a Category 1A recommendation. I am not aware of

any in vivo studies assessing different time intervals for changing the tubing after administration of propofol.

Page 47, line 1053-1063: you state "The optimal time for routine replacement of IV administration sets has been examined in a number of well-controlled studies and meta-analyses". This is a bit of overstatement. None of these studies used CR-BSI as the endpoint, as the number of patients required for such a study is huge. Thus, they have all used indirect methods (something you have not considered robust in other areas) of fluid or line contamination. I think it would be appropriate to list as one of the limitations of all of these studies, that they all have used indirect methods to assess the impact of IV administration set change and have not used CR-BSI. Also, realize that you have given this a Category 1A recommendation. Have you been similarly accepting of use of indirect measure outcome measurement in other areas? A large number of interventions that have used CR-BSI as the outcome measure (antibiotic lock/flush, use of prophylactic antibiotics during catheter insertion, CHG-impregnated patch, etc.) that have more robust studies (including randomized controlled trials) have not been given a Category 1A recommendation. Evidence should be the driver for the level of recommendation. That does not appear to be the case in a number of places in this guideline.

Also, please add the study by Highsmith et al assessing changing such tubing at 24 vs. 48 hours (the first to evaluate this and the first to stop the study and using an indirect method—contamination-when they realized that to evaluate the impact of CR-BSI would require a huge sample size.

Page 47, lines 1066-1068: I do not believe any of these references provide data to support this recommendation. Several assessed split septum only, devices that required an end-cap, or only in vitro studies. I believe that the manufacturer's and INS recommend changing the needleless connector every 24 hours (like you recommend for administration sets) if blood transverses the connector.

Page 47, lines 1069-1071: I do no t believe that any of these references provide data to support this recommendation.

Page 47, lines 1072-1073: This study only addresses home infusion therapy, not inpatient use of neddleless connectors.

Page 48, line 1074-1076: The references cited do not support this recommendation. You should be referencing in vitro studies by Menyhay and Maki (reference 346) and add reference Kaler et al (JAVA 2007). These studies show: that a 5-10 second wipe with 70% alcohol is insufficient and a CHG cap was effective in disinfecting selected mechanical valve needleless connectors with 10^8cfu/ml inoculum (Menyhay) and that a 15-30 second scrub with either 70% alcohol or 2% CHG with alcohol is sufficient for disinfection of selected mechanical valve needleless connectors (at least if the inoculum is 10^5 cfu/ml or less) (Kaler W et al.). I do not believe that there are any data to indicate that CHG is "preferred" as you indicate. Thus, your recommendation should list either

70% alcohol or CHG (with or without alcohol) AND that the application should include time (>15 secs) and scrubbing the hub not just wiping it. I am not aware of any randomized controlled trials or in vivo studies assessing any methods of needleless connector disinfection. Furthermore, you did not give a recommendation for use of antiseptic/antimicrobial locks or flushes and mentioned that there was not an FDA approved product. I do not believe that CHG (although used by some and assessed in these in vitro studies) is FDA-approved as a disinfectant, but rather only as an antiseptic.

Page 48, lines 1078-1079: I believe this recommendation needs to be re-worded given the available data. The data show increased CR-BSI risk with either negative pressure (Jarvis et al CID-December 16, 2009 or Fields (reference 339) or positive pressure (references 336, 337, 338, and 339) luer access mechanical valve needleless connectors. I believe the data would support a Category 1B recommendation that of the needleless connectors that have been evaluated, split septum technologies are associated with a lower risk of CR-BSI than negative or positive pressure leur access mechanical valve needleless connectors.

Page 48, lines 1064-1079: There should be a recommendation to use closed systems and another recommendation that given the high rate of contamination of stopcock, that they be avoided if at all possible.

This section needs considerable re-writing. First, there should be a discussion of the different types of needleless connectors (split septum; negative, positive or neutral leur access mechanical valve needleless connectors). Second, there should be an acknowledgement that there are very few data on occlusion rates with any of these connectors (one study actually showed an increase in partial or total occlusions with use of saline vs. heparin and positive pressure mechanical valve needleless connectors). Third, it should be pointed out that many, if not most, positive pressure or displacement mechanical valve needleless connectors have positive pressure on syringe/line connection or disconnection, but that is followed by negative pressure (the amount [mm] varies with the connector). So, if the purpose of positive pressure/displacement connector is to keep blood from entering the distal end of the IV catheter, they may not accomplish what they are designed to. Given the virtual absence of data on occlusions with different types of needleless connectors, it would be very, very difficult for clinicians to select a needleless connector on the basis of occlusion data. Fourth, it should be pointed out that the outbreaks associated with needleless connectors, initially were when the first split septum (Baxter Interlink) was introduced. The outbreaks were associated with the use of TPN and infrequent cap changes. Once aseptic technique and cap change frequency was improved, adverse events associated with their use decreased. Then, after the introduction of positive pressure/displacement mechanical valve needleless connectors, CR-BSI outbreaks have occurred (even when enhanced infection control practices were used—see Jarvis CID Dec 16, 2009). More recently, there has been CR-BSI outbreaks associated with negative pressure mechanical valve needleless connectors (Fields, Toscano-ICHE 2009, Jarvis-CID-Dec 16, 2009). Fifth, you should differentiate in vitro studies (many of which are comparisons with open systems or use of stopcocks--already known to have higher rates of contamination and CR-BSI--from in vivo studies. Most of

the in vitro studies are microbial ingress studies (or in several papers inoculation of the septum and then swabbing it or infusing media through it). It is not clear how well these reflect the clinical situation. Similarly, the study by Seymore (reference 331) is a comparison of contamination in one negative pressure mechanical valve (changed every 72 hrs) vs. stopcocks; the contamination rates were similar. Seventh, you may want to comment on the fact that by using needleless connectors rather than stopcocks, one can better maintain a closed system (something that you do not mention in this document, but that has been recommended for decades). Given the large amount of data from V. Rosenthal and others on the use of open systems internationally and the fact that he/they have shown repeatedly a reduction in CR-BSI with the introduction of closed systems, I believe you should comment on the value of closed systems in this guideline. Eighth, please add references by Cookson et al (ICHE 1998;19:23-27), Danzig (JAMA 1995;273:1962-64), Kellerman (J Peds 1996;129:711-7), Toscano (AJIC 2009;37:327-34), and Harnage (JAVA 2007;12:4-8). Twelfth, you should point out that the risk of CR-BSI may be linked to difficulty cleaning the access surface, gaps around the plunger, opaque housing that hides incomplete flushing, internal mechanisms that obscure the fluid path, confusion over the correct clamping-disinfection sequence (it is different with negative vs. positive pressure mechanical valves), inadequate flushing, or failure to replace the device per protocol (only INS has a recommendation). Other factors that may influence mechanical valve needleless connector CR-BSI infection risk is whether blood is infused or withdrawn through the connector, whether TPN or lipid emulsion is infused through it, how many clinicians manipulate the connector, etc.

Page 49, lines 1108-1110: You state: "When the devices are used according to manufacturers' recommendations,…..they do not substantially affect the incidence of CRBSI (328-335)." This is statement that was in the 2002 CDC IV Guideline and I strongly believe that current data show this is not true. See the following publications: Hall K. et al. abstract from SHEA 2004, your references 337, 336, 338, 339, and Jarvis CID In Press 2009. I believe theses data show unequivocally that the use of negative or positive pressure luer access mechanical valve needleless connectors (even with enhanced infection control practices—see Jarvis CID 2009 In Press) are associated with increased CR-BSI risk, even if infection control practices are enhanced compared to the split septum period (see Jarvis et al 2009)

Page 49, lines 1116-1117: This is not accurate. Include the reference by Kaler et al (JAVA 2007) and change this to indicate that mere wiping with alcohol (5-10 secs) is inadequate, but <u>scrubbing</u> (15-30 secs) with alcohol or CHG (with or without alcohol) is effective in disinfecting these mechanical valve needleless connectors.

Page 50, line 1126: The Maragakis reference (reference 338) did not address this issue.

Page 50, line 1126-1128: There are no published studies at all; much less any randomized controlled trials. Reword to indicate no in vitro or in vivo studies have been published and there are no data to indicate that these devices will reduce the risk of CR-BSI.

Page 51, line 1140 :: Add Grohskopf LA et al. NEJM 2001;344:1491-1497 that illustrates the negative impact of combining contents of left over single use vials in the clinical setting. Again, this is a Category 1A based on dogma not data. No randomized controlled trials have assessed this. In this section, you should make a strong recommendation for the use of:
a) pharmacy admixture of medications/fluids;
b) use of single use unit dose medications/fluids;
and
c) use of pre-filled syringes for flushing catheters, etc.

In this section, you might want to emphasize that use of single dose or pharmacy prepared unit dose medications and elimination of admixture of infusates/medications at the bedside by nurses or physicians reduces the risk of CR-BSI associated with extrinsic contamination.

You might also want to reference: V. Rosenthal's publications, Al-Rabea AA, et al. in ICHE 1998;19:674-679, and Moore KL et al in PIDJ 2005;7:590-594 that illustrate the magnitude of this problem in international settings.

Page 51, lines 1144-1148: Not sure that these 1-2 references support a Category 1A recommendation. Again common sense and dogma, but no randomized controlled studies. One of these references (352) is an in vitro study. The other reference (351) is experience in one anesthesia department.

Use might also want to mention that the use of pre-filled syringes decrease this risk associated with admixture at the bedside.

Page 52, lines 1173-1240: It might be more useful to those implementing these recommendations to be more specific with the components of the bundle (an insertion and a maintenance bundle) that should be the basic elements of any CR-BSI prevention program. Given the success of implementing such bundles, to duck the issue by indicating that no randomized controlled trials have assessed these, seems ingenuous. In previous areas you have discounted large numbers of randomized control trials (CHG impregnated sponge), so why now raise this. The single institution, CHCA (Jefferies ICHE 2009), NACHRI, and Keystone Projects (realize that hospitals varied in other practices—BioPatch, maintenance bundle, impregnated catheters, etc.) all show the impact implementation of insertion and maintenance bundles can have. You should be mandating that they be implemented in all ICUs today and that the CDC, AHRQ funding be used to assess the efficacy of these interventions (with IV/PICC teams) in the non-ICU population. In addition, you have not stressed the importance of CEO, nursing/physician ware/unit directors, and clinician accountability. A change in culture from inevitability to zero tolerance is needed. This guideline, if you strongly recommend recommendations on the basis of the data can markedly improve patient safety.

Your recommendation (page 52, line 1175-1177) is very generic and does not provide the specificity that most infection preventionists need in order to fully implement it. You

should be much more directive in your recommendation. Exactly what are the minimum elements that should be implemented (similar to the SHEA compendium)? How would an infection preventionist at a 50-150 bed hospital take this to their hospital administrator and use it to force change? I am also not sure why this is listed last. Most people will never make it this far and it will not be seen or implemented.

Pages 58-60: Update to 2009 or 2010 data, so these tables will not be 3-4 years old at the time this guideline is published.

Page 62: All financial disclosures, including government funding, speaker's bureaus, grant funding, etc. should be included.

I look forward to seeing your revised Guideline.

Sincerely yours,

William R. Jarvis, M.D.
President, Jason and Jarvis Associates
December 2, 2009